

### **REMARKS**

The Office Action mailed July 18, 2002 has been received and the Examiner's comments carefully reviewed. Claims 1, 15, 19, 20, 22-24 have been amended. Applicants have included herewith a document entitled, "VERSION WITH MARKINGS TO SHOW CHANGES MADE" to indicate how the claims have been amended. Claims 34-56 have been added. No new subject matter has been added. Claims 26 and 27 have been cancelled without prejudice. Claims 1-25 and 28-56 are currently pending.

Applicants submit that the amended and newly presented claims are supported by the specification. In particular, support for amended claim 24 can be found in the specification at least at page 26, lines 6-27.

For at least the following reasons, Applicants respectfully submit that the pending claims are in condition for allowance.

#### **Rejection of Claims Under § 112, Second Paragraph**

The Examiner rejected claims 2-13, 15-23, 25-27, and 29-33 under 35 U.S.C. § 112, second paragraph. The Examiner objected to certain terms and phrases used in the claims. Applicants respectfully traverse this rejection.

The Examiner objected to the phrase "a blood level oxygen" in claims 2, 25, 27, and 29. The Examiner correctly inferred that this phrase refers to the level of oxygen located outside of the membrane of the red blood cell in the blood of the subject. The various locations of oxygen are described in a section of the specification starting at page 6 and ending at page 8. In particular, blood level of oxygen is described at page 6, line 28, through page 7, line 14, referring to compartment two. Therefore, this phrase is well defined in the specification as filed.

The Examiner objected to the recitation in claims 15, 19, 22, and 23 of the phrase "being adapted and configured to/for". The present amendment either deletes this phrase from the claims or substitutes the term "configured".

The Examiner objected to each of claims 22 and 23 for not positively reciting a component. These claims have been amended to include positively recite the components.

Claim 26 has been canceled, which renders this rejection moot for this claim.

Accordingly, it is believed that the amended claims fully comply with § 112, second paragraph, and withdrawal of this rejection is respectfully requested.

#### **Rejection of Claims Under § 101**

The Examiner rejected claims 1-14 and 24-27 under 35 U.S.C. § 101 as claiming the same invention as claims 1-18 of U.S. Patent 6,037,181 (the '181 patent). Applicants respectfully traverse this rejection.

Independent claim 1 has been amended and differs from each claim of the '181 patent. Thus, each of dependent claims 2-14 also differs from each claim of the '181 patent. Independent claim 24 has been amended and differs from each claim of the '181 patent. Thus, dependent claim 25 also differs from each claim of the '181 patent. Claims 26 and 27 have been canceled, which renders this rejection moot for these claims.

Accordingly, it is believed that the amended claims fully comply with § 101, and withdrawal of this rejection is respectfully requested.

#### **Obviousness-Type Double Patenting Rejection**

The Examiner rejected claims 28-33 under the judicially created doctrine of obviousness-type double patenting over claims 1-3 and 6-8 of U.S. Patent No. 6,037,181. Applicants respectfully traverse this rejection.

However, if this rejection remains when each of the pending claims are otherwise in condition for allowance, Applicants will, if appropriate, submit a terminal disclaimer.

#### **Rejection of Claims Under § 102(b)**

The Examiner rejected claims 15, 17, 19-20 and 22-23 under 35 U.S.C. § 102(b) as being anticipated by Page et al. (from Chapter 9-Exp. Simulation of Oxygen Transport in Microvessels). Applicants respectfully traverse this rejection, but have amended claims 15, 19, 20, and 22 to advance this application to allowance. Applicants reserve the right to pursue the original subject matter via a continuation application. Claim 15 is the only independent claim of this group.

Claim 15 has been amended to clarify that the red blood cell transport system of the claimed apparatus includes a sample receiving system for receiving a sample of a red

blood cell and a pump to transport a red blood cell from the sample receiving system to the gas exchange system. Claim 15 also now clarifies that the gas exchange system includes a gas permeable tubing for diffusing the gas from the chamber to a red blood cell contained within the gas permeable tubing.

Applicants submit herewith as Exhibit A, a marked up copy of Page's FIG. 9.1 including Applicants' added reference letters. Referring Exhibit A, Page discloses an apparatus having capillary A. The capillary is in fluid communication with a feed reservoir B by a feed pipette C. The capillary A is also in fluid communication with a withdrawal reservoir D by withdrawal pipette E. In use, a solution F containing blood cells is exposed to gas within the feed reservoir B. A syringe pump (not shown) is operated to draw the solution F from the feed reservoir B to the capillary A. The sample is examined under a microscope G and then drawn to either the syringe pump or drain.

Page does not disclose an apparatus as recited in claim 15. First, Page does not disclose a system having both a sample receiving system and a gas exchange system. In contrast, Page discloses a glass capsule feed reservoir B having a gas inlet, a gas vent, and a solution drain (i.e. a gas exchange system). Page simply does not disclose a sample receiving system. It is noted that the feed reservoir B cannot be construed as both a sample receiving system and a gas exchange system. In particular, claim 15 clarifies that a pump transports a red blood cell from the sample receiving system to the gas exchange system. Therefore, the feed reservoir B of Page cannot be characterized as both elements between which the pump provides fluid communication.

yes, gas  
exchange  
occurs  
in  
capillary  
of page

Second, Page also fails to disclose a gas permeable tubing located within the housing for diffusing gases from the gas exchange chamber to a red blood cell contained within the gas permeable tubing. In contrast, Page discloses a feed reservoir B that contains both the solution F, and the gases to which the solution F is directly exposed. The solution F is not diffused while contained within a gas permeable tubing, as recited in claim 15, rather is diffused while contained within the reservoir B (i.e. housing).

Because Page fails to disclose a sample receiving system, a gas exchange system, and a pump that provides fluid transport therebetween, or in the alternative, a gas exchange system including a gas permeable tubing for diffusing gases to a red blood cell

contained therein, Applicants submit that claim 15 is patentable. Claims 17, 18-20 and 22-23 depend upon claim 15 and are therefore also patentable.

Accordingly, based on the foregoing differences, it is believed that the reference cited in this rejection neither teaches nor suggests the presently claimed apparatus, and withdrawal of this rejection is respectfully requested.

#### **Rejection of Claims Under § 103(a)**

The Examiner rejected claims 16, 18, and 21 under 35 U.S.C. § 103(a) as being obvious over Page et al. in view of what is asserted to be Applicants' admitted prior art. Claims 16, 18 and 21 depend upon claim 15. In view of the remarks above regarding independent claim 15, further discussion regarding the independent patentability of dependent claims 16, 18, and 21 is believed to be unnecessary. Applicants submit that dependent claims 16, 18, and 21 are in condition for allowance.

Accordingly, based on the foregoing differences, it is believed that the references cited in this rejection neither teach nor suggest the presently claimed apparatus, and withdrawal of this rejection is respectfully requested.

#### **Newly Presented Claims**

New claim 34-54 depend upon claim 15. In light of the comments above with regards to the patentability of claim 15, applicants respectfully submit that dependent claim 34-54 are patentable. However, Applicants provide the following comments for further consideration.

New claim 34 depends upon claim 15 and relates to the gas exchange system. Claim 34 is patentable over Page as Page fails to disclose a system that permits gas exposure to successive blood samples without cross-contamination between the samples. Rather, the apparatus of Page would introduce cross-contamination of successive samples as the feed reservoir B (i.e. housing) is in direct contact with the solution F.

New claims 35-38 depend upon claim 15 and relate to the sample receiving system. As discussed previously, Page fails to disclose a sample receiving system as characterized.

New claims 39-41 depend upon claim 15 and relate to the gas permeable tubing. Applicants submit that Page fails to disclose a flat or rectangular shaped gas permeable tubing (claims 39 and 40) or a removable gas permeable tubing (claim 41).

New claims 42-46 depend upon claim 15 and relate to the gas exchange system. Applicants submit that Page fails to disclose the recited atmospheric concentrations.

New claims 47-50 depend upon claim 15 and relate to the oxygen level detector. Applicants submit that Page fails to disclose dual spectrophotometric detectors (claim 47) or a light source having an absorption free wavelength of at least 358 nm, about 660 nm, and about 805 nm (claims 48-50).

New claims 51-54 depend upon claim 15 and relate to the control system. Applicants submit that Page fails to disclose a measuring system that measure the amount of diffusion at least once every 15 seconds (claim 51), and other system components as recited in claim 52-54.

#### Summary

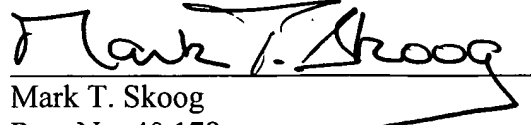
It is respectfully submitted that each of the presently pending claims is in condition for allowance and notification to that effect is requested. The Examiner is invited to contact Applicants' representative at the below-listed telephone number if it is believed that prosecution of this application may be assisted thereby.

Although certain arguments regarding patentability are set forth herein, there may be other arguments and reasons why the claimed invention is patentably distinct. Applicants reserve the right to raise these arguments in the future.

Respectfully submitted,

MERCHANT & GOULD P.C.  
P. O. Box 2903  
Minneapolis, Minnesota 55402-0903  
612.332.5300

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Mark T. Skoog  
Reg. No. 40,178  
MTS:KAF:PSTtdm

**VERSION WITH MARKINGS TO SHOW CHANGES MADE**

**In the Claims**

Claims 1, 15, 19, 20, and 22-24 have been amended as follows:

1. (Amended) A method for determining a patient's blood oxygen transport [and lipid level], comprising [the steps of]:
  - obtaining a blood sample from the patient;
  - measuring a rate of oxygen diffusion across a membrane of a red blood cell of the blood sample; and
  - correlating the measured rate with:
    - established levels of blood lipid to determine the patient's blood lipid level;
    - susceptibility to angina observed in a control population, or in the patient, at the measured rate;
    - established levels of blood lipid to determine the patient's relative or absolute blood lipid level; or
    - combination thereof.

15. (Amended) An apparatus for measuring diffusion of oxygen across a red blood cell membrane comprising an oxygen level detector, a gas exchange system, and a red blood cell transport system;

the red blood cell transport system being [adapted and] configured [for] to transport[ing] a fluid containing red blood cells through the gas exchange system and the oxygen level detector, the red blood cell transport system comprising:

- a) a sample receiving system configured to take in a sample of a red blood cell;
- b) a pump configured to transport a red blood cell from the sample receiving system to the gas exchange system and the oxygen level detector;

the gas exchange system [being adapted and] configured to couple to a gas source and to exchange a gas with the fluid containing the red blood cells at a rate faster than the rate at which the gas diffuses across a membrane of the red blood cell, the gas exchange system comprising:

- a) a housing defining a gas inlet, a gas outlet, and a chamber;
- b) a gas permeable tubing at least partially located within the housing for diffusing the gas from the chamber to a red blood cell contained within the gas permeable tubing;

the oxygen level detector [being adapted and] configured [for] to detect[ing] oxygen levels in a red blood cell or in fluid surrounding the red blood cell, the oxygen level detector comprising:

- a) a light source producing light having an absorption free wavelength;
- b) at least one filter;
- c) photopickups to detect the transmission of light at the absorption free wavelength; and

a control system comprising a microprocessor electronically coupled to the oxygen level detector, the gas exchange system, and the red blood cell transport system to operably derive amounts of oxygen levels in a red blood cell.

19. (Amended) The apparatus of claim 15, wherein the gas exchange system comprises a closed loop diffusion system; the closed loop diffusion system comprising [a] the gas permeable tubing and [a] the housing.; the gas permeable tubing having a lumen effective for containing red blood cells; the housing being adapted and configured for containing to contain successive samples of gases.]

20. (Amended) The apparatus of claim 15, wherein the pump of the red blood cell transport system comprises [a pump] an aspirator.

22. (Amended) The apparatus of claim 15, [wherein] further comprising a cartridge-type insert; the cartridge-type insert and the red blood cell transport system

[comprise a] comprising the gas permeable tubing[, the gas permeable tubing being arranged and configured to exchange a gas with a fluid containing red blood cells]; the cartridge-type insert being [arranged and configured for inserting] configured to be inserted into the apparatus, [removing] and removed from the apparatus[, and] for disposal.

23. (Amended) The apparatus of claim 15, [wherein] further comprising a modular system insert and [the red blood cell transport system comprise] a receiving and diffusion system, the modular system insert and the red blood cell transport system comprising the receiving and diffusion system; the receiving and diffusion system being [arranged and] configured to exchange a gas with a fluid containing red blood cells; the modular system insert being arranged and configured for inserting into the apparatus, removing from the apparatus, and disposal.

24. (Amended) A method for determining a patient's susceptibility to angina, comprising [the steps of]:  
obtaining a blood sample from the patient;  
measuring a rate of oxygen diffusion across a membrane of a red blood cell of the blood sample; [and]  
correlating the measured rate with the susceptibility to angina observed in a control population, or in the patient, at the measured rate; and  
correlating the measured rate with residence time of the blood in the heart during stress.

New claims 34-56 have been added.